

the pathophysiology of congestive heart failure (CHF). Recently, the immune system has also been implicated in the progression of CHF. Therefore, we investigated whether plasma soluble intercellular adhesion molecule (sICAM)-1 levels are elevated in patients with CHF by means of enzyme-linked immunosorbent assay. Furthermore, we assessed whether the plasma sICAM-1 concentration could provide supplementary prognostic information in addition to that obtained from standard clinical and biochemical variables previously known to be associated with a high mortality. The plasma concentration of sICAM-1, atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and norepinephrine (NE) were measured in 102 patients with CHF (left ventricular ejection fraction (EF) < 0.45; NYHA class II–IV). The patients were then monitored for a follow-up period of over 18 months. The plasma sICAM-1 concentration increased with the severity of the CHF (normal, 150 ± 10 ng/ml; NYHA class II, 228 ± 19 ng/ml; NYHA class III–IV, 292 ± 20 ng/ml), and there was a significant negative correlation between the plasma sICAM-1 concentration and the EF ($r = -0.34$; $p < 0.001$). A Cox proportional hazard analysis was performed to determine if the plasma levels of sICAM-1, ANP, BNP, and NE were the independent significant predictors of the EF. High concentrations of sICAM-1 ($p = 0.01$) and BNP ($p = 0.001$), but not ANP nor NE, were shown to provide independent prognostic predictors in 102 CHF patients.

These findings indicate that the plasma concentration of sICAM-1 is elevated in CHF and that high plasma levels of sICAM-1 can be independent prognostic predictor in patients with CHF. Taken together, these findings suggest that the immune system, as well as neurohumoral activation play a significant role in the pathophysiology and progression of CHF.

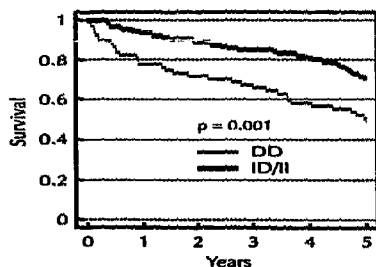
901-78 The DD Genotype of the ACE-Gene Is Associated With Increased Mortality in Idiopathic Heart Failure

Bert Andersson, Christer Sylvén.

Div. of Cardiology, Wallenberg Laboratory for Cardiovascular Research, Sahlgrenska University Hospital, Göteborg; Div. of Cardiology, Dept. of Medicine, Karolinska Institute at Huddinge Hospital, Stockholm, Sweden

An insertion (IT)/deletion (D) polymorphism in the angiotensin II-converting enzyme (ACE) gene has been associated with increased levels of ACE. To relate this polymorphism to survival and cardiac function we investigated a group of patients with idiopathic congestive heart failure (CHF) ($n = 193$), recruited from the world's largest unselected CHF population ($n = 2711$). DNA from white blood cells was isolated and the occurrence of an IT or a D allele in the ACE-gene was analysed by PCR technique. The patients were investigated by echocardiography. Five-year survival data was available for all patients.

Results: Patients with genotype DD ($n = 67$) 0.6 had a significantly poorer survival as compared with the ID/II group ($n = 126$), as assessed by a Cox multivariate regression analysis ($p = 0.001$). The only difference in cardiac function between the two groups was an increase in left ventricular mass in the DD group (153 ± 57 vs 134 ± 44 g/m²; $p = 0.02$).



Conclusion: The DD genotype of the ACE-gene polymorphism implicated an increased mortality in patients with idiopathic CHF. The increase in left ventricular mass provides a possible pathophysiological link between an increased ACE-activity and mortality.

HEMODYNAMICS/SHOCK/ASSIST DEVICES

901-79 Use of the Intra-aortic Balloon Pump as an Aortic Cross-clamp to Maximize Effectiveness of CPR in Humans

Roger H. Coletti, Bruce J. Haik, Joseph G. Wiedermann. Hackensack Medical Center, Hackensack, NJ

Experimental data in the dog model has suggested that coronary blood flow during cardiopulmonary resuscitation (CPR) is markedly augmented by abdominal aortic cross-clamping. In an attempt to apply this data to CPR in

humans, we have developed a novel use of the intra-aortic balloon pump (IABP), which allows it to work as a functional aortic cross-clamp. Using a conventional recent-model Datascope™ IABP, settings of "1" on the inflation cycle and "4" on the deflation cycle are selected. The IABP is then set to "internal trigger" at 1:1, with the ECG disconnected. These settings will keep the IABP inflated almost constantly, allowing a brief deflated period for limb perfusion while maximizing coronary blood flow.

This IABP strategy was used in 7 consecutive patients (over a 1 year period) who suffered cardiac arrest requiring CPR while undergoing coronary intervention, and failed to respond to conventional balloon-pumping. All 7 patients experienced cardiac arrest (non-arrhythmic) secondary to acute closure of a major epicardial vessel, with no immediate response to prompt re-opening of the culprit vessel, and no significant hemodynamic improvement with conventional use of the IABP for ≥ 5 min. All 7 patients displayed ST elevations ≥ 3 mm in the distribution of the culprit artery. After documenting absence of hemodynamic improvement despite standard ACLS protocol, CPR, and ≥ 5 min. of conventional IABP use, the IABP was set to cross-clamp mode and CPR was continued. All 7 patients exhibited normalization of ST segments and restoration of hemodynamic stability within 8 minutes of combined application of IABP cross-clamp and CPR with manual compression. All seven patients were safely discharged from the hospital within 10 days post-procedure.

Conclusions: IABP settings can be modified in such a way as to allow the balloon pump to act as a functional aortic cross-clamp. Use of this novel IABP cross-clamp technique can maximize the effectiveness of CPR during cardiac arrest, presumably by augmenting coronary blood flow. IABP cross-clamp can produce patient salvage even after the failure of standard ACLS/CPR protocols combined with conventional balloon-pumping. Use of the IABP cross-clamp technique is probably of greatest benefit in cases of cardiac arrest secondary to coronary flow obstruction, such as in acute closure during percutaneous coronary interventions.

901-80 Systemic Capillary Leak Syndrome. Long-Term Follow Up

Naem K. Tahirkheli, Philip R. Greipp. Mayo Clinic, Rochester, MN

Systemic Capillary Leak Syndrome (SCLS) is a rare idiopathic disorder, characterized by hypotension, hemoconcentration and marked shifts of plasma (10–70%) from intravascular to extravascular space. A monoclonal gammopathy is almost always found. Complications include anasarca, compartment syndromes resulting in rhabdomyolysis, myocardial infarction, hypovolemic shock, renal shut-down and frequently death. We reported our initial successful experience with a combination of terbutaline and aminophylline. We now report further follow up on this regimen in a larger cohort.

Methods: 7 patients of SCLS were seen at Mayo Clinic in the last 15 years, ages 28 to 65 years and then have been followed from 3 months to 14 years. All have been treated long-term with terbutaline and aminophylline. Steroids were used variably.

Results: 1 patient expired due to hemodynamic compromise and steroid related complications. 1 patient discontinued aminophylline and terbutaline after 11 years of treatment and is without recurrence for the last 3 years. Recurrence of attacks were usually treated with increase in dosage of aminophylline and terbutaline. We were able to obtain theophylline levels in at least 2 patients during and after the recurrences. These were noted to be sub-therapeutic despite compliance and were probably secondary to tachyphylaxis. Higher doses were effective.

Conclusions: Empiric treatment with aminophylline and terbutaline prevents severe and fatal attacks. Recurrences due to sub-therapeutic levels and tachyphylaxis are effectively treated with increases in doses.

HYPERTENSION

901-81 Left Ventricular Function and Remodeling in Stage I Hypertension: The Treatment of Mild Hypertension Study

Philip R. Liebson, Sinda Dianzumba, Greg Grandits, Ronald J. Prineas, Richard H. Grimm, Jr for the TOMHS Research Group. Rush Medical College, Chicago, IL; University of Minnesota, Minneapolis, MN

Left ventricular (LV) systolic performance and hemodynamic measures were evaluated for various types of LV hypertrophy (LVH) patterns in 844 subjects (S) with Stage I hypertension [mean BP 140/91] without heart disease, using M-mode echocardiography. LVH was determined using LV mass index ≥ 134 g/m² for men and ≥ 110 g/m² for women. A total of 130 had LVH. Categories of remodeling with LVH included disproportionate septal hypertrophy (DSH) [$n = 10$]; septal/posterior wall ratio ≥ 1.6 ; concentric hypertrophy (CH) [$n = 43$]; relative wall thickness (RWT) ≥ 0.45 ; eccentric dilated hypertrophy (EDH) [$n = 10$]; RWT < 0.45 and LV dimension ≥ 3.1 cm/m² [$n = 10$]; and

eccentric non-dilated hypertrophy (ENDH) [$n = 67$]: RWT < 0.45 and LV dimension < 3.1 cm/m². Comparing LVH v. non-LVH S, stroke volume index (SVI), stroke work index (SWI), minute work index (MWI) and end systolic stress (ESS) were significantly greater $p < 0.01$ in the non-LVH group. Total peripheral resistance (TPR) and ESS/ESVI, a measure of inotropic state, was greater in the LVH group ($p < 0.001$). Comparisons of LVH remodeling subgroups indicated significant intragroup differences for SVI, SWI, MWI, TPR, peak systolic stress (PSS), ESS, and ESS/ESVI. SVI, MWI and MWI, PSS and ESS were highest in the EDH group, and TPR and ESS/ESVI were highest in the DSH group. No inter- or intragroup differences were noted for fractional shortening or circumferential fiber shortening. These results demonstrate that in Stage I hypertensives, differences in LV performance measures and hemodynamics are present in comparison of LVH v. non-LVH, and by type of LVH remodeling.

901-82 Effects of Transdermal Estradiol-17 β on Hypertension in Postmenopausal Women

Giuseppe Mercuro, Sandra Zoncu, Angelo Cherchi. *Institute of Cardiology, University of Cagliari, Sardinia, Italy*

Estrogen replacement therapy (ERT) with estradiol-17 β (E₂ β) has effects on cardiovascular haemodynamics and protects against the development of both cardiovascular diseases and stroke.

We studied 10 postmenopausal women (mean age 52.2 ± 2.4 years; E₂ β plasma concentrations < 25 pg/ml; time-lapse from menopause 2–4 years) with mild hypertension (SBP 172 ± 19 , DBP 99 ± 5 mmHg) and without target organ complications. The women showed no evidence of cardiovascular or other systemic diseases. All subjects complained of menopausal symptoms. None was taking hormone replacement therapy nor assuming antihypertensive drugs or other medications which would affect cardiovascular activity. According to a randomized, double-blind protocol they received patches of transdermal E₂ β (rated to assure plasma levels of E₂ β > 75 pg/ml) or matched placebo, with crossover after a 1 week washout period. A 24-hour ambulatory BP monitoring was performed at baseline and after E₂ β or placebo administration. Results were as follows:

	Mean daytime			Mean nighttime		
	HR (b/min)	SBP (mmHg)	DBP (mmHg)	HR (b/min)	SBP (mmHg)	DBP (mmHg)
Placebo	76 ± 10	174 ± 21	99 ± 8	64 ± 5	164 ± 11	90 ± 10
E ₂ β	75 ± 11	$151 \pm 13^*$	$91 \pm 8^*$	64 ± 8	$142 \pm 15^{**}$	$81 \pm 5^*$

Data are means \pm SD; * $p < 0.05$; ** $p < 0.01$ vs. placebo

Menopause ERT is a physiological rather than a pharmacological approach. Our preliminary data show that ERT have beneficial effects in both lowering elevated BP levels and maintaining a uniform BP control over 24 hours. The finding that HR was unchanged after E₂ β administration seems to suggest an immediate effect of the hormone on the arterial wall. In our opinion, ERT could be considered when significant changes in BP take place in the postmenopausal period and are associated with signs or symptoms of hormone deprivation.

901-83 Echocardiographic Left Ventricular Hypertrophy and the Angiotensin-Converting Enzyme-Gene in Elderly Hypertensives

Wilfred F. Heesen, Frank W. Beltman, Yigal M. Pinto, Pieter A. de Graeff, Wiek H. van Gilst, Andries J. Smit, Johan F. May, Betty Meyboom-de Jong, Kong I. Lie. *Departments of Cardiology, Medicine, Clinical Pharmacology and General Practice, University of Groningen, and Groningen Hypertension Service, The Netherlands*

Purpose: To evaluate the association of the deletion (DD)-type gene for the angiotensin-converting enzyme with left ventricular mass index (LVMI) in elderly with newly-found diastolic (DH) and isolated systolic hypertension (ISH) from a population survey, compared with normotensive controls (Con).

Introduction: The DD-genotype is associated with increased risk for myocardial infarction mainly in normotensives, less clearly in hypertensives. In DH, more electrocardiographic (EKG) LV hypertrophy is found in patients with the DD-genotype. In this report, LVMI is measured in hypertensives and normotensives with echocardiography, what is more sensitive than the EKG.

Methods: The ACE-genotype was determined with the polymerase-chain reaction in 45 DH-patients (4x diastolic BP (DBP) ≥ 95 mmHg) and 57 ISH-patients (4x systolic BP ≥ 160 ; DBP < 95 mmHg), and in 67 normotensive controls from a population survey (age 60–74 yrs). LVMI was calculated from posterior wall thickness (PWT) and the end-diastolic dimension (EDD). Also, LV diastolic function (early to atrial (E/A) filling ratio) was measured.

Results:

	genotype	n	BP(mmHg)	LVMI(g/m ²)	PWT(mm)	EDD(mm)	E/A
DH	I/I/D	32	161/99	93.1	10.1	44.6	0.89
	DD	13	157/98	81.6*	9.2*	43.9	0.88
ISH	I/I/D	42	175/88	99.9	10.1	45.4	0.82
	DD	15	176/87	89.4(*)	10.1	43.7(*)	0.82
Con	I/I/D	53	135/81	73.0	8.5	43.8	0.88
	DD	14	138/82	72.2	8.3	43.7	0.86

* $p < 0.05$, (*) $p < 0.10$. Age and gender: no differences.

Conclusions: In both hypertensive groups, patients with the DD-genotype show a smaller increase of echocardiographic LVMI, despite comparable levels of blood pressure and LV diastolic function. This may explain why the DD-genotype is more associated with cardiovascular risk in normotensives rather than in hypertensives.

INTRALUMINAL ULTRASOUND/ANGIOSCOPY

901-84 High Resolution Vascular Imaging With Optical Coherence Tomography

Mark E. Brezinski, Guillermo J. Tearney, Stephen A. Boppart, Brett E. Bouma, Michael R. Hee, Eric A. Swanson, James F. Southern, James G. Fujimoto. *Mass. General Hosp. and MIT, Boston, Mass.*

Optical coherence tomography (OCT) is a recently developed technology which uses reflected infrared light to produce micron scale imaging. OCT is analogous to conventional ultrasound using infrared light rather than acoustical waves. In this work, we directly compare muscular arteries (medium and large), elastic arteries, and venous bypass grafts for their imaging properties. Arterial and venous tissue were obtained immediately postmortem. Two dimensional cross sectional images of these tissues were generated by an OCT system with a 1300 nm diode. After imaging, the microstructure was confirmed by routine histologic processing of the tissue. The axial resolution of OCT was demonstrated to be 16 ± 1 μ m. The dynamic range was 109 dB. Penetration was possible completely through normal coronary arteries but only partially through aorta or carotid arteries. The internal and external elastic membrane could be demonstrated in muscular arteries. The intima-media and media-adventitia borders were well demarcated in muscular arteries. OCT represents a promising new technology for intraarterial imaging due to its high resolution, ability to generate contrast within arterial walls, and the fiber optic design which is compatible with intravascular catheters.

901-85 Can Radiofrequency Data Analysis of Intravascular Ultrasound Accurately Characterize Coronary Atherosclerosis?

M. Paulina Ramo, Timothy Spencer, George R. Sutherland, Donald M. Salter, Peter Kearney, David Lamb, T.R.D. Stuart Shaw, Norman W. McDiicken, Raimund Erbel¹, Peter Fitzgerald¹. *University of Edinburgh, Edinburgh, UK; ¹ RF-Tissue Collaborative Project, Edinburgh, UK*

To determine whether spectral analysis of the unprocessed radiofrequency (RF) signal from an IVUS scanner offers advantages over videodensitometric analysis of vessel wall morphology, 57 regions of interest (ROI) were analysed from 5 post-mortem pressure perfused (80 mmHg) coronary vessels imaged in a saline bath. These were imaged at 30 MHz and the RF data was digitised at 250 MHz. ROI were identified from scan-converted images and the relative amplitudes of different frequency components were analysed. The spectra were normalised by data acquired from a perfect specular reflector, enabling spectral slope (dB/MHz) to be calculated over a given bandwidth (17–42 MHz). 3-dimensional (3-D) RF images were constructed and compared with 3-D comparative histology derived from microscopy and radiologic techniques. Dense fibrotic (DFP) and calcified plaques (CaP) showed similar mean backscattered energies (mBE), but the gradient of the spectral slope (Gr) was higher in CaP (-0.43 ± 0.1) than in DFP (-0.29 ± 0.1) ($p = 0.004$). Loose fibrotic plaque (LFP) was identified from moderate fibrosis (MFP) and DFP with mBE, Gr and y-axis intercept, MFP from DFP with Gr and intercept ($p < 0.001$). MBE was higher in smooth muscle cells (SMC -18.2 ± 0.9) than in the foam cells (-24.4 ± 0.1 dB) and in LFP with lipid (-23.2 ± 0.4 dB) ($p < 0.001$). These preliminary results demonstrate that spectral slope may be used to identify different plaque types and for quantitative analysis of vessel wall morphology.